# EXHIBIT 25

Higher pre-pregnancy BMI was strongly correlated with an increase in many of the pollutants measured in breast milk in our cohort. Post-pregnancy BMI was measured in other settings and found to be a significant predictor of the likelihood of having higher concentrations for the sum of DDT and DDE, HCB, and ß-HCH while leading to lower concentrations for PCB levels (Schade et al., 1998). Mothers who were more highly exposed to PCB had a lower weight gain during pregnancy than non-exposed women (Fein et al., 1984). For the Faroese mothers, a negative correlation could be shown between weight gain and mercury in mother's hair and most of the tested other POPs (β-HCH, HCB, DDT, DDE, and trans-nonachlor) in breast milk. A higher weight gain during pregnancy may lead to a dilution of POPs previously accumulated, thus giving lower concentrations of the named contaminants in breast milk. To answer this question in detail the mother's load with pollutants has to be known before pregnancy.

The influence of alcohol consumption during pregnancy on the reduction of mercury concentrations in mothers is well known (Weihe et al., 1996; Dunn et al., 1981). However, mercury in hair in this study increased significantly with mother's consumption of alcohol during pregnancy. Because of the low alcohol intake levels, this association is likely to be spurious and not an indication of toxicokinetic interactions. In German and Canadian breast milk samples consumption of spirits (alcoholic beverages) led to an increase of ß-HCH and HCB (Schade et al., 1998; Dewailly et al., 1996). The reason for the relationship is not clear. Alcohol abuse can induce chronic liver damage, which may in turn reduce the biotransformation rate of the measured chemicals. Alternatively, alcohol could increase absorption of organochlorines by raising the solubility of the substances in gastrointestinal fluids. Another and more likely explanation could be that alcohol intake is related to specific eating habits, especially to a diet containing more fat (Schade et al., 1998). In the presented study, DDT was higher in alcohol-consuming mothers. Also the ratio DDT/DDE in these mothers was significantly higher than the one in teetotal mothers which either could be caused by the fact that the life style of mothers who consume alcohol leads to a higher ingestion of DDT or that the conversion to DDE is delayed by a hampered or changed metabolism. Mothers who drank alcohol reported a higher amount of whale meat, a higher number of meals with dried whale meat, and a lower number of fish meals per week consumed during pregnancy. This supports the hypothesis that alcohol consumption is related to a different diet, which increases their load of pollutants.

Smoking showed no significant association with organochlorine compounds in breast milk also reported by other authors (Schade et al., 1998; Vartiainen et al., 1998). According to Lackmann ΣPCB (also true for the all single congeners except PCB 180) and HCB increase in a smoking mother (more in active than in passive smoking mothers) (Lackmann et al., 2000). Again, any toxicokinetic impact is questionable.

The average dioxin and PCB concentration in human milk increased with the education of the mother (Vartiainen et al., 1998). The same was seen in the Faroese cohort while the mercury concentration in maternal hair decreased with higher education of the parents, and also most of the POPs were lower if the father had a higher school education. With higher occupation and / or profession of parents an increase of POPs was found as also described by Jacobson (Jacobson et al., 1990), probably caused by the highly significant

positive correlation between maternal age and occupational or professional status of both parents.

Low score in school education and low score in mother´s occupation are correlated with a higher consumption of whale meat during pregnancy while no influence on the number of fish meals per week could be seen. There are two possible explanations for the observation: either the lower education led to an ignorance of governmental recommendation concerning the consume of whale products or the living place of the mother functioned as confounder for a lower school education and occupation on one side and a higher availability of whale meat on the other side. A connection of social data like school education or present occupation of parents with the place of mother´s residence was not yet possible.

That preference and availability of whale products influence the load with contaminants became clear when correlating nationality and exposure data: higher concentrations of nearly all contaminants were found in Faroese women who can be assumed to be used to the consumption of whale products and seabirds and to have a better access to both.

*6.2.4.2 Non-neurological characteristics of the infants*

An apparently positive influence of all pollutants on birth weight was seen. After splitting the PCB-congeners into the individual congeners that were measured in breast milk it became clear that mainly the mono-ortho congener PCB-105 increases the birth weight, while PCB-153 (a di-ortho PCB) leads to a significant reduction of birth weight. In boys, the changes in both directions were stronger than in girls. Additionally a negative effect of DDE, HCB, and trans-nonachlor could be shown. A negative effect of POPs, especially of PCB on birth weight corresponds to the experience of several other authors (Fein et al., 1984; Schade et al., 1998; Brouwer et al., 1995; Patandin et al., 1998). However, because of collinearity these effects may be difficult to disentangle. The linear regression model explaining birth weight resembles well the one for another Faroese cohort (Grandjean et al., 2001), but some additional factors influencing the birth weight could be identified: maternal weight, diabetes of mother, and mother´s nationality, the last one probably reflecting the preference or availability of some food items or the presence of other ingredients in the dietary which differ in native people and foreigners. Thus, in our previous study, we showed the strong effect of polyunsaturated fatty acids present in fish oil, but these parameters were not assessed in the present study.

For head circumference, the same pattern of positive influences (especially the significantly positive correlation with HCB, PCB-105, PCB 118, DDT, and trans-nonachlor were found. The length of boys measured at the neurological examination decreased in dependence of the concentration of β-HCH, HCB, PCB-153, PCB-156, and DDE. In girls no significant effects on birth weight and head circumference were seen; solely their length increased significantly with increasing concentrations of contaminants.

Possible mechanisms by which PCB-105, PCB-118, HCB, 4,4´-DDT, and trans-nonachlor may affect birth weight and head circumference may relate to a growth-hormone-like effect of the substances or in their effect similar to other hormones.

The effects of the contaminants as hormone active agents (DDE acting antiandrogenic, some of the PCB-congeners and DDT causing estrogen-like effects) might explain why reactions to the pollutants differ between boys and girls. Altogether the girls appear less vulnerable than the boys. The incidence of hypospadias and cryptorchism that might be a sequel of disturbances in the early development of male sex organs caused by hormone active agents was too low to be tested statistically.

No significant correlation between either diet or one of the pollutants and length of gestation was found in this study, but was reported in other studies in the Faroe and elsewhere (Fein et al., 1984; Grandjean et al., 2001). But the concentration of fatty acids in maternal or cord serum that are responsible for a prolongation were not available for this cohort.

Our data suggest a relationship between sex and parity as well as sex and concentration of contaminants: the higher the parity, the higher the percentage of boys. First pregnancies resulted in more girls than boys, after the second child the boys outweighed the girls. The proportion of boys increased with each pregnancy. This may confirm the findings of other authors: Mocarelli and Brambilla reported an excess of female offsprings of parents who were exposed to high concentrations of dioxin after the Seveso accident (Mocarelli et al., 1996). Brouwer et al (Brouwer et al., 1995), found fewer boys than expected born to fishermen wives from the Swedish East Coast, whose pooled blood samples were found to have higher PCB levels than those of the Swedish West Coast. PCB levels and the concentration of POPs in breast milk were lower in primi-parae in our study. Still more girls than boys were born to primi-parae. Probably not only dioxin but a mixture of several substances are responsible for this phenomenon.

*6.2.4.3 Neurological outcome*

The interpretation of the neurological results is made difficult by several potential obstacles: For the second half of the study period higher NOS scores were achieved. This might be caused by (1) a higher percentage of children examined by A (48.2% versus 57.6%) who tended to give higher scores for the examination during the later part of the study or (2) because both examiners increased their scores during the study. As already discussed above (6.2.3.2.) it is not easy to get comparable results for the NOS if different persons carry out the examination. Thus the cohort had to be separated for most of the analyses of the neurological outcome. Many other factors can be of major impact on the performance, some of them like environmental temperature and interval between last meal and examination could be identified. But there well might be some important unknown factors that change the result of the examination.

An overall negative correlations was found between all exposure variables and NOS for the complete cohort and the subcohort B. In the subcohort the correlation often reached significance level especially if controlled for gestational age. The most important substances that caused a reduction of the NOS were HCB, PCB-105 (as well as the sum of the three measured mono-ortho PCB-105, 118, and 156), trans-nonachlor, and 4,4-DDT. For the subcohort A mostly a positive influence of the substances on the neurological performance of the infant was found. Only the concentration of mercury in maternal hair (very weakly correlated) showed a negative effect on the neurological outcome of the newborn. A positive correlation between prenatal exposure to POP is against the experience from former studies (Committee

on Hormonally Active Agents in the Environment, 2001; Huisman et al., 1995; Rogan et al., 1986; Steuerwald et al., 2000). Because the examination and the scoring for the NOS is a highly subjective, it has to be assumed that the explanation for the unexpected results in the subcohort A was caused by spurious variation. Unfortunately a regular interrater-reliability control or a control of the examination technique of the examiners, which could have helped to reduce differences, was not possible.

Postural tone cluster score was weakly reduced by most of the contaminants. This confirms the findings of other authors who also described a decrease of muscle ton with increasing concentrations of PCB (Huisman et al., 1995; Fein et al., 1984; Rogan et al., 1986). The impact of the pollutants on the reflex cluster score was stronger: for the subcohort B a highly significant negative correlation between reflex score all tested substances except MeHg and musk xylene was apparent. In other words: POPs led to a hyporeflexia in this group of infants. Rogan saw a negative influence of PCB on reflexes (Rogan et al., 1986). and DDE levels in breast milk as low as 4 μg/g lipid can suppress reflexes in newborns (AMAP, 1997). The eight infants who were exposed to such a high concentration of DDE in our study, had a lower reflex cluster score (and NOS) but the difference from the other infants did not reach significance. Mercury was positively associated with abnormal reflexes in boys, but not in girls (hyperreflexia). Hyperreflexia and exaggerated deep tendon reflexes were observed in boys with high mercury exposures during pregnancy, but the present study could not confirm this association (WHO, 1990).

As to the anthropometric results, the associations with the contaminants differed in boys and girls, e.g. β-HCH increases the probability for the diagnosis "hypokinesia", but reduces it in girls (both correlations were not significant). After controlling for some of the covariates which were found to have an impact on the NOS (namely corrected age in days at the neurological examination, environmental temperature during examination, and log10-transformed maternal pre-pregnancy BMI), the NOS in girls was negatively related to mercury (in the B subcohort), but boys showed a weak positive correlation. On the other side a significant (in the B subcohort) an influence of nearly all other pollutants could be shown in boys while for girls no correlation of the same substances on NOS was seen. A possible mechanism that might explain the phenomen was mentioned in section 6.2.4.2.

#### *6.2.4.4 Diet and exposure variables*

As has been known for some time (Grandjean et al.,1992) the amount of whale meat consumed during pregnancy is the best predictor for maternal MeHg exposure. Blubber and to a much lesser degree fish may add some more mercury to the maternal load. Any form of blubber - dried or fresh – seems to be the major source not only for PCB but also for DDT, DDE, and trans-nonachlor. The consumption of fulmar showed positive correlations to PCB, DDT, DDE, and trans-nonachlor. High levels of PCB were already described to be most likely the effect a diet of sea mammals, fatty fish, and perhaps eggs from seabirds (AMAP, 1997). It is known that also other seabirds, especially those which eat fish, have high levels of PCB and DDT. The puffin is one of them, and it is frequently consumed in the Faroe. The contamination of migratory seabirds like the fulmar often originates from pollution of their wintering areas. The concentration of pollutants in the eggs of the birds often approaches the levels where effects like embryo deformities and failing of hatching might occur (AMAP, 1997). The questionnaire used

did not ask about consumption of seabird eggs. However, of the seabirds eaten by the mothers, the correlation with fulmar exeeded those for other seabirds. Recommendations about the consumption of seabirds and eggs might be considered as a consequences of these findings.

The consumption of all different whale products – meat or blubber, fresh or dried – is interrelated, i.e. those who have access to whale products are likely to use them all. Those who eat fulmar tend also to eat other seabirds, but only the consumption of dried whale meat is significantly correlated to the number of fulmars eaten during pregnancy. Probably this is a sign of traditional lifestyle that leads to a very high exposure to the potentially harmful substances.

Fish meals as such seem to be less important when looking for the sources of contaminants. The number of fish meals correlates with mercury in maternal hair and milk, DDT, DDE, and trans-nonachlor. Of the PCB-congeners the concentration of PCB-105 and PCB-118 increased with the number of fishmeals per week, but not the other congeners.

High HCB-concentration resulted from the consumption of whale meat, blubber, and fulmar but not from fish. Musk xylene showed mainly negative associations. Again this might reflect a certain traditional life style that reduces the use and contact with preparation containing musk xylene.

Consumption of other meat, (e.g. chicken, lamb or beef), serves as a protective factor against the exposure of the infant and foetus by the potentially harmful substances as indicated by negative correlations with the pollutants.

Maternal smoking and smoking of partner is found more often in families where the mother reported that they had eaten whale meat and / or blubber on two consecutive days. This might suggest an overall unhealthy life style where recommendations for an optimal outcome of pregnancy are unknown or ignored.

*6.2.4.5 Comparison of present exposure data with those from earlier studies*
The geometric average of hair-mercury in about 1,000 Faroese women of children born in 1986 and 1987 was 4.3 µg/g, with 130 samples above 10 µg/g; the maximum was 39.1 µg/g. Only 5% of the Faroese women had hair-mercury concentrations below 1 µg/g (Grandjean, 1992). Compared to this cohort, slightly lower overall mercury concentrations were found in a second cohort that was created in 1994 and 1995 with geometric means of 4.1 µg/g (Steuerwald et al., 2000). In the present data a geometric mean of 2 µg/g was found. Now only 5% of the samples exceeded a concentration of 10 µg/g and 18% were below 1 µg/g. The highest load with a concentration of 32.7 µg/g did not differ much from the one reported for the earliest cohort. Thus mercury concentration has clearly decreased since the establishment of the first cohort, probably as result of changed recommendations for the population about the consumption of whale products.

Differences in the load with PCB are much smaller due to the longer half-lives of these compounds which despite of changed dietary habits will take longer time to decrease. For the second cohort (for the first cohort only PCB-levels in umbilical cord for half of the children were available) ΣPCB in breast milk from day 4-5 had a geometric mean of 1.52 µg/g lipid (total range 0.07-18.5

μg/g) (Steuerwald et al., 2000) which is nearly identically to the values resulting from this cohort (1.33 μg/g lipid with a total range of 0.08-17.6 μg/g lipid). However, as the analyses were conducted by the same laboratory, the slight decrease indicated may reflect a real change.

In the second cohort, DDE in maternal milk reached a geometric mean of 0.87 μg/g lipid, the interquartile range was 0.49 – 1.55 μg/g, with a total range of 0.05 – 13.7 μg/g (Steuerwald et al., 2000). If compared with the values of the present cohort, a slight decline in this contaminant as well was found, with 0.60 μg/g for the geometric mean, an interquartile range of 0.36 – 0.99 μg/g, and a total range of 0.06 – 11.35 μg/g.

Whether the described decline of MeHg, ΣPCB, and 4,4´-DDE is solely caused by the changed recommendation about the consumption of whale meat and blubber, a higher awareness of the population about the potential harm of whale-products especially for the foetus and young infant, or whether this is an effect of reduced load of the whales themselves after implementation of strict regulations and bans of some of the substances cannot be decided by these data. In addition, maternal age may be considered as a covariate, the mothers from cohort 2 now being about 5 years older at the time of the generation of the present cohort 3.

### 6.2.5 Conclusions

Marine food / traditional food provides many benefits: Marine mammals and fish are rich in polyunsaturated fatty acids. A diet high with PUFA has been associated with lower risk for heart disease. Whale skin and other marine foods are rich in selenium. Selenium may perhaps reduce the toxic effect of mercury, may increase the body's antioxidant defence, and may protect against cancer and possibly against heart disease. High levels of vitamin A are found in animal liver and blubber. In general, traditional diets therefore provide a strong nutritional base for health (AMAP, 1997). But the growing foetus is exposed to contaminants in the womb, and the levels in the mother´s body will determine its dose of persistent organic pollutants. By the time a woman knows that she is pregnant, she can only partially influence this dose by changing her food habits. Most of the exposure comes from persistent organic pollutants she has accumulated in her body since she was born. An important way to reduce fetal exposure to POPs is therefore to develop dietary advice for girls, women of child-bearing age, and pregnant women to promote the use of less contaminated local food to help reduce POP intake (AMAP, 1997).

Realizing the hazard resulting from the present contaminations and as a consequence of the findings of studies in the Faroes, new recommendations on the consumption of whale products were issued by the government in 1998. Adults should refrain from having more than one or two lunches of whale meat (corresponding to 300g whale meat each second week) or blubber per month. Girls and women should not eat blubber at all before the end of the reproductive period. Women who intend to get pregnant during the next three months, women who are pregnant or those who are breastfeeding should not eat any whale meat at all. Livers and kidneys of whale should not be eaten by anyone at all (Heilsufrøðiliga Stravsstovan, 1998). Whale meat contains about 1.9 mg/kg. i.e. much more than mercury levels in Faroese fish. This is the background for the above-mentioned recommendation for whale meat. Because of the beneficial effects of fish consumption, the long-term goal

needs to be a reduction in the concentration of MeHg in seafood rather than a replacement of fish in the diet by other foods. In the interim, the best method of maintaining fish consumption and minimizing Hg exposure is the consumption of fish known to have low mercury concentrations (Committee on the Toxicological Effects of Methylmercury, 2000).

Another easy recommendation should be added for nursing mothers: while a higher weight gain during pregnancy leads to a reduction of the concentration of contaminants in the body, this advance has to be weighed against the higher incidence of complications during delivery, lower Apgar scores and other disadvantages of the maternal weight gain. A reduction of maternal weight during the lactation period leads to a very high concentration of all compounds in breast milk, and therefore should be avoided (Institut für Wasser-, Boden- und Lufthygiene des Bundesumweltamtes, 1999).

PCB and HCB have carcinogenic and teratogenic properties, and tumor-promoting properties if applied together with tobacco-specific carcinogens (Lackmann et al., 2000). Therefore tobacco smoking together with eating whale products and seabirds (probably also eggs of seabirds) should be strongly discouraged in the whole population.

Further effects especially those of the hormone active agents will have to be examined in some years.

### 6.2.6 Summary

Effects of prenatal exposure to methyl mercury and persistent organic pollutants originating from marine food were studied. Data collection took place during a two-year period and involved a cohort of 500 mother-infants pairs. Information about socioeconomic and obstetrical conditions and the dietary habits of the mother during pregnancy was recorded. As outcome parameters length of gestation, growth and sex were recorded. Neurological performance was tested at the adjusted age of about two weeks. Exposure was determined by analyzing maternal hair for mercury and transitional breast milk for persistent organic pollutants.

An adverse influence of these contaminants on the outcome variables could be shown. Differences in results in boys and girls are in agreement with the ability of several of the substances to mimic or disturb the function of sex hormones.

When comparing the exposure in the present study with previous established Faroese cohorts it could be shown that contamination with mercury now amounts to only half of the exposure 15 years ago. Concentration of POPs in breast milk were almost unchanged since 1994.

Further activities of health authorities are necessary to reduce the still high exposure of the population. In addition to whale meat and blubber, attention should also be paid to fulmars and perhaps also other seabirds as sources of exposure.

### 6.2.7 Appendix

#### *6.2.7.1 Abbreviations*

| | |
|---|---|
| BMI | body mass index (weight [in kg] / height [in m]$^2$) |
| $X^2$ | Chi-square |
| DDE | 4,4'-dichlorodiphenyldichloroethene |
| DDT | 4,4'-dichlorodiphenyltrichloroethane |
| FDA | Food and Drug Administration |
| HAA | hormonally active agent |
| HCB | hexachlorobenzene |
| ß-HCH | beta-hexachlorocyclohexane |
| Hg | mercury |
| IUPAC | International Union of Pure and Applied Chemistry |
| MeHg | methylmercury |
| NOS | neurological optimality score |
| OCC | organochlorine compounds |
| OFC | occipito-frontal circumference (head circumference) |
| OOS | obstetric optimality score |
| PCB | polychlorinated biphenyls |
| POP | persistent organic pollutants |
| ppb | parts per billion = 1 μg / kg = 1 ng / g |
| ppm | parts per million = 1 mg / kg = 1 μg / g |
| PUFA | polyunsaturated fatty acid |
| ΣPCB | (sum of PCB 138, 153 and 180) x 2 |

#### *6.2.7.2 Tables*

TABLE 6.2.21 LIST OF ITEMS INCLUDED IN THE OBSTETRICAL OPTIMALITY SCORE

| Variable | Criteria for optimality |
|---|---|
| *A: Social background* | |
| Education of partner[&] | More than elementary |
| Education of mother's father* | More than elementary |
| Marital state at time of delivery* | Married (or permanently living together) |
| Parenthood course* | Participated in parenthood course |
| Race and nationality | [Not defined for the study cohort] |
| Education of mother[&] | More than elementary |
| Smoking of partner | Not smoking |
| Family history of congenital anomalies | No |
| Previous baby with congenital anomalies | No |
| Previous legal abortion | No |
| Height of mother | 160 – 180 cm |
| Age of mother | 20 – 31 years |
| BMI (weight / height$^2$) of mother | 18.8 – 24.2 |
| *B: Non-obstetrical conditions during pregnancy* | |
| Smoking of mother | No smoking during whole pregnancy |
| Illness first trimester | No |
| Surgical therapy during gestation | No |
| Family history of diabetes | No |
| Diabetes (including gestational) of gravida | No |
| Heart disease | No |
| Epilepsy | No |

| | |
|---|---|
| Hypertension (at or above 90 mm Hg diastolic) | No |
| Other disease | No |
| *C: Obstetrical past history* | |
| Preterm delivery | None |
| Late abortion (16-28 weeks) | None |
| Early abortion (<16 weeks) | Not more than one |
| Late fetal or neonatal loss | None |
| Caesarian section | None |
| Instrumental delivery | None |
| Hypertension in pregnancy | No |
| Placental abruption | None |
| Other complications | None |
| Placenta praevia | None |
| Intrauterine growth retardation | No |
| Parity | One |
| Previous infertility | No |
| Induction of ovulation | No |
| *D: Obstetrical aspects of pregnancy* | |
| Vaginal bleeding | No |
| Proteinuria | No |
| Pre-eclampsia | No |
| Acetonuria* | No |
| Anemia in mid-trimester (Hb < 6.8 mmol/l) | No |
| Anemia in third trimester (Hb < 6.8 mmol/l) | No |
| Early hypertension (diastolic pressure > 80 mm Hg) | No |
| Uncertain or unreliable date of last menstrual period | No |
| Weight gain during pregnancy | 8 – 15 kg |
| Other complications e graviditate | No |
| Rhesus sensitization | No |
| *E: Diagnostic and therapeutic measures* | |
| Frequency of prenatal care | 9 – 15 visits |
| Number of admissions including for delivery | One |
| Oral Glucose Tolerance Test carried out | No |
| Amniocentesis | No |
| Placental function tests, CTG etc. | *Yes* |
| Drugs prescribed or taken prior to 16 th week | No |
| Drugs prescribed or taken after 16 th week | No |
| Cerclage | No |
| *F: Parturition* | |
| Complications during labor | None |
| Instrumental delivery including caesarian section | No |
| Resentation at birth | Cephalic |
| Perineal lacerations | Episiotomy |
| Duration of first period | 10 hours or less |
| Duration of second period | 50 min or less |
| Amniotic fluid | Clear |

| | |
|---|---|
| Start of labor | Spontaneous |
| Augmentation | No |
| Time between rupture of membranes and birth | 6 hours or less |
| Sedation or analgesia | None |
| *G: Neonatal condition immediately after birth* | |
| Duration of gestation | 37 to 42 weeks completed |
| Birth weight | More than P10[&] or less than P95[&] |
| First cry | Immediately |
| Apgar score 1 minute | 8 – 10 |
| Apgar score 5 minutes | 9 – 10 |
| Congenital anomalies | None |
| Transferred to neonatal ward | No |

* : No information available for this cohort, therefore always scored optimal
& : For further information, see text in chapter 2.5.5

TABLE 6.2.22 CORRELATION COEFFICIENTS (SPEARMAN) BETWEEN DIFFERENT GROUPS OF PERSISTENT ORGANIC POLLUTANTS IN BREAST MILK

| Spearman's rho | Mercury | HCB | β-HCH | 4,4'-DDT | 4,4'-DDE | Ratio DDT/DDE | Trans-nonachlor | Musk xylene |
|---|---|---|---|---|---|---|---|---|
| PCB 105 | 0.383** | 0.835** | 0.374** | 0.848** | 0.786** | 0.318** | 0.828** | -0.003 |
| PCB 118 | 0.341** | 0.894** | 0.427** | 0.861** | 0.879** | 0.218** | 0.929** | -0.030 |
| PCB 138 | 0.274** | 0.869** | 0.435** | 0.806** | 0.914** | 0.078 | 0.944** | -0.012 |
| PCB 153 | 0.273** | 0.872** | 0.433** | 0.779** | 0.899** | 0.054 | 0.920** | -0.019 |
| PCB 156 | 0.236** | 0.853** | 0.469** | 0.695** | 0.811** | 0.035 | 0.867** | -0.074 |
| PCB 180 | 0.255** | 0.834** | 0.398** | 0.714** | 0.837** | 0.032 | 0.887** | -0.034 |
| ΣPCB | 0.269** | 0.869** | 0.428** | 0.777** | 0.895** | 0.056 | 0.927** | -0.020 |
| Sum of three MO-PCB[&] | 0.334** | 0.907** | 0.444** | 0.850** | 0.878** | 0.200** | 0.931** | -0.036 |
| | | | | | | | | |
| HCB | 0.356** | | | | | | | |
| β-HCH | -0.021 | 0.589** | | | | | | |
| 4,4'-DDT | 0.399** | 0.802** | 0.351** | | | | | |
| 4,4'-DDE | 0.317** | 0.805** | 0.379** | 0.851** | | | | |
| Ratio DDT/DDE | 0.215** | 0.222** | 0.072 | 0.513** | 0.037 | | | |
| Trans-nonachlor | 0.345** | 0.859** | 0.360** | 0.864** | 0.877** | 0.881** | | |
| Musk xylene | -0.009 | - 0.065 | 0.027 | 0.030 | 0.093* | 0.091* | -0.030 | |

* : Significant at the 0.05-level (two-tailed)
**: Significant at the 0.01-level (two-tailed)
& : Some of the three measured mono-ortho PCB-congeners (IUPAC numbers 105, 118, and 156)

TABLE 6.2.23 CORRELATION COEFFICIENTS (SPEARMAN) BETWEEN DIETARY HABITS AND MERCURY (IN MOTHER'S HAIR) AND DIFFERENT POPs (IN BREAST MILK) FOR ALL P-VALUES ≤ 0.100. IN THE SECOND LINE IN EACH ROW, THE P-VALUES SIGNIFICANCE ARE GIVEN. THOSE REACHING A SIGNIFICANCE LEVEL OF 0.05 ARE WRITTEN IN **BOLD** NUMBERS.

| | MeHg (hair) | HCB | β-HCH | Musk xylene | DDT | DDE | Ratio DDT/DDE | Trans-nonachlor |
|---|---|---|---|---|---|---|---|---|
| Number of meals with whale meat (N=261) | 0.571<br>**0.000** | 0.116<br>0.061 | N.s. | N.s. | 0.177<br>**0.004** | 0.125<br>**0.043** | N.s. | 0.167<br>**0.007** |
| Total amount of whale meat (N=217) | 0.556<br>**0.000** | 0.136<br>**0.045** | N.s. | N.s. | 0.214<br>**0.002** | 0.152<br>**0.025** | N.s. | 0.202<br>**0.003** |
| Number of meals with blubber (N=256) | 0.362<br>**0.000** | 0.221<br>**0.000** | N.s. | N.s. | 0.313<br>**0.000** | 0.248<br>**0.000** | 0.160<br>**0.010** | 0.307<br>**0.000** |
| Total amount of blubber (N=238) | 0.355<br>**0.000** | 0.252<br>**0.000** | N.s. | N.s. | 0.342<br>**0.000** | 0.275<br>**0.000** | 0.170<br>**0.009** | 0.328<br>**0.000** |
| Number of other meals with dried whale meat (N=257) | 0.202<br>**0.001** | 0.114<br>0.068 | N.s. | N.s. | 0.182<br>**0.003** | 0.141<br>**0.024** | n.s. | 0.122<br>0.051 |
| Number of other meals with dried blubber (N=258) | 0.215<br>**0.000** | 0.158<br>**0.011** | N.s. | N.s. | 0.367<br>**0.000** | 0.291<br>**0.000** | 0.228<br>**0.000** | 0.284<br>**0.000** |
| Number of fish meals per week (N=256) | 0.250<br>**0.000** | N.s. | N.s. | N.s. | 0.147<br>**0.018** | 0.138<br>**0.028** | N.s. | 0.143<br>**0.022** |
| Number of meals with fulmar (N=258) | 0.213<br>**0.001** | 0.207<br>**0.001** | N.s. | -0.146<br>**0.019** | 0.169<br>**0.007** | 0.147<br>**0.018** | N.s. | 0.234<br>**0.000** |
| Number of meals with other seabirds (N=257) | 0.128<br>**0.040** | 0.110<br>**0.079** | N.s. | N.s. | 0.137<br>**0.028** | 0.106<br>0.091 | N.s. | 0.116<br>0.063 |
| Total number of meals with seabirds (N=256) | 0.194<br>**0.002** | 0.184<br>**0.003** | N.s. | N.s. | 0.179<br>**0.004** | 0.155<br>**0.013** | N.s. | 0.213<br>**0.001** |
| Number of meals with other meat per week (N=253) | -0.174<br>**0.005** | -0.146<br>**0.020** | -0.142<br>**0.024** | N.s. | -0.104<br>0.100 | -0.101<br>0.108 | N.s. | N.s. |

TABLE 6.2.24 CORRELATION COEFFICIENTS (SPEARMAN) AND P-VALUES BETWEEN DIFFERENT PCB CONGENERS AND DIETARY HABITS DURING PREGNANCY (FOR $P \leq 0.1$). IN THE SECOND LINE IN EACH ROW, THE P-VALUES FOR THE TWO-TAILED SIGNIFICANCES ARE GIVEN. THOSE REACHING A SIGNIFICANCE LEVEL OF 0.05 ARE WRITTEN IN **BOLD** NUMBERS.

| PCB-congener number | 105 | 118 | 138 | 153 | 156 | 180 | Σ PCB |
|---|---|---|---|---|---|---|---|
| Number of meals with whale meat (N=261) | 0.162<br>**0.009** | 0.126<br>**0.041** | 0.121<br>0.051 | N.s. | N.s. | N.s. | n.s. |
| Total amount of whale meat (N=217) | 0.179<br>**0.008** | 0.157<br>**0.021** | 0.153<br>**0.025** | N.s. | N.s. | N.s. | 0.109<br>0.109 |
| Number of meals with blubber (N=256) | 0.246<br>**0.000** | 0.269<br>**0.000** | 0.246<br>**0.000** | 0.212<br>**0.001** | 0.157<br>**0.012** | 0.178<br>**0.004** | 0.214<br>**0.001** |
| Total amount of blubber (N=238) | 0.279<br>**0.000** | 0.298<br>**0.000** | 0.278<br>**0.000** | 0.249<br>**0.000** | 0.189<br>**0.003** | 0.206<br>**0.001** | 0.247<br>**0.000** |
| Number of other meals with dried whale meat (N=257) | 0.140<br>**0.025** | 0.137<br>**0.029** | 0.129<br>**0.039** | 0.132<br>**0.034** | 0.108<br>0.085 | 0.101<br>0.106 | 0.122<br>0.050 |
| Number of other meals with dried blubber (N=258) | 0.231<br>**0.000** | 0.258<br>**0.000** | 0.239<br>**0.000** | 0.196<br>**0.002** | 0.145<br>**0.020** | 0.166<br>**0.008** | 0.203<br>**0.001** |
| Number of fish meals per week (N=256) | 0.131<br>**0.037** | 0.133<br>**0.033** | 0.103<br>0.100 | N.s. | N.s. | N.s. | N.s. |
| Number of meals with fulmar (N=258) | 0.254<br>**0.000** | 0.241<br>**0.000** | 0.203<br>**0.001** | 0.213<br>**0.001** | 0.213<br>**0.001** | 0.196<br>**0.002** | 0.207<br>**0.001** |
| Number of meals with other seabirds (N=257) | 0.172<br>**0.006** | 0.176<br>**0.005** | 0.111<br>0.076 | 0.127<br>**0.041** | 0.115<br>0.066 | 0.114<br>0.068 | 0.117<br>0.060 |
| Total number of meals with seabirds (N=256) | 0.242<br>**0.000** | 0.246<br>**0.000** | 0.192<br>**0.002** | 0.203<br>**0.001** | 0.202<br>**0.001** | 0.191<br>0.052 | 0.197<br>**0.002** |
| Number of meals with other meat per week (N=253) | N.s. | -0.118<br>0.061 | N.s. | N.s. | -0.116<br>0.066 | N.s. | N.s. |

N : Number of answers that were available for analyses

TABLES 6.2.25 –6.2.30
Bivariate / partial correlations between anthropometric data and exposure variables; p-values of significant correlations are written in bold letters

TABLE 6.2.25 BIVARIATE CORRELATION BETWEEN BIRTH WEIGHT AND EXPOSURE DATA

| Birth weight | Spearman´s rho | | | P-values | | |
|---|---|---|---|---|---|---|
| | All infants (N=500) | Boys (N=267) | Girls (N=233) | All infants (N=500) | Boys (N=267) | Girls (N=233) |
| Mercury | 0.062 | 0.073 | 0.016 | 0.168 | 0.235 | 0.807 |
| HCB | 0.076 | 0.144* | -0.009 | 0.088 | 0.019 | 0.891 |
| β-HCH | 0.004 | 0.043 | -0.024 | 0.931 | 0.483 | 0.715 |
| PCB-118 | 0.103* | 0.159** | 0.041 | 0.021 | 0.009 | 0.537 |
| PCB-153 | 0.043 | 0.107 | -0.026 | 0.334 | 0.082 | 0.690 |
| PCB-105 | 0.141** | 0.202** | 0.073 | 0.002 | 0.001 | 0.269 |
| PCB-138 | 0.053 | 0.112 | -0.015 | 0.239 | 0.066 | 0.821 |
| PCB-156 | 0.052 | 0.113 | -0.040 | 0.250 | 0.066 | 0.830 |
| PCB-180 | 0.046 | 0.110 | -0.025 | 0.309 | 0.074 | 0.699 |
| ΣPCB | 0.047 | 0.110 | -0.022 | 0.290 | 0.074 | 0.733 |
| Sum of three mono-ortho PCB (105+118+156) | 0.099* | 0.157* | 0.033 | 0.027 | 0.010 | 0.614 |
| 4,4'-DDT | 0.080 | 0.163** | -0.019 | 0.074 | 0.008 | 0.767 |
| 4,4'-DDE | 0.044 | 0.096 | -0.013 | 0.328 | 0.119 | 0.848 |
| Ratio DDT/DDE& | 0.087 | 0.183** | -0.036 | 0.053 | 0.003 | 0.586 |
| Trans-nonachlor | 0.074 | 0.132* | 0.004 | 0.100 | 0.032 | 0.951 |

* : Significant correlation (2-tailed significance)
** : Highly significant correlation (2-tailed significance)
& : Pearson correlation

TABLE 6.2.26 BIVARIATE CORRELATION BETWEEN HEAD CIRCUMFERENCE AND EXPOSURE DATA AT NOS

| Head circumference at NOS | Spearman´s rho | | | P-value | | |
|---|---|---|---|---|---|---|
| | All infants (N=499) | Boys (N=267) | Girls (N=232) | All infants (N=499) | Boys (N=267) | Girls N=232) |
| Mercury | 0.105* | 0.099 | 0.073 | 0.019 | 0.108 | 0.267 |
| HCB | 0.057 | 0.126* | -0.011 | 0.206 | 0.039 | 0.872 |
| β-HCH | -0.043 | 0.023 | -0.082 | 0.343 | 0.708 | 0.213 |
| PCB-118 | 0.067 | 0.111 | 0.048 | 0.136 | 0.071 | 0.466 |
| PCB-153 | 0.027 | 0.068 | 0.005 | 0.541 | 0.267 | 0.940 |
| PCB-105 | 0.098* | 0.150* | 0.067 | 0.029 | 0.014 | 0.313 |
| PCB-138 | 0.036 | 0.075 | 0.015 | 0.422 | 0.220 | 0.918 |
| PCB-156 | 0.021 | 0.052 | 0.000 | 0.642 | 0.396 | 0.995 |
| PCB-180 | 0.036 | 0.068 | 0.013 | 0.421 | 0.269 | 0.846 |
| ΣPCB | 0.031 | 0.070 | 0.011 | 0.487 | 0.251 | 0.846 |
| Sum of three mono-ortho PCB (105+118+156) | 0.061 | 0.105 | 0.040 | 0.174 | 0.088 | 0.547 |
| 4,4'-DDT | 0.058 | 0.101 | 0.039 | 0.194 | 0.101 | 0.558 |
| 4,4'-DDE | 0.038 | 0.088 | 0.009 | 0.393 | 0.152 | 0.891 |
| Trans-nonachlor | 0.063 | 0.100 | 0.037 | 0.158 | 0.104 | 0.579 |

* : Significant correlation (2-tailed significance)

TABLE 6.2.27 HEAD CIRCUMFERENCE AND EXPOSURE DATA: PARTIAL CORRELATION, CONTROLLED FOR CORRECTED AGE IN DAYS AT NOS; FOR EXPOSURE VARIABLES, THE LOG10-TRANSFORMED VALUES WERE USED

| Head circumference at NOS (controlled for age) | Partial correlation coefficient | | | P-value | | |
|---|---|---|---|---|---|---|
| | All infants (N=499) | Male (N=267) | Female (N=232) | All infants (N=499) | Male (N=267) | Female (N=232) |
| Mercury | 0.108* | 0.099 | 0.077 | 0.016 | 0.109 | 0.244 |
| HCB | 0.065 | 0.100 | 0.017 | 0.147 | 0.105 | 0.802 |
| β-HCH | -0.046 | 0.003 | -0.075 | 0.305 | 0.690 | 0.255 |
| PCB-118 | 0.100* | 0.115 | 0.084 | 0.025 | 0.062 | 0.201 |
| PCB-153 | 0.057 | 0.076 | 0.031 | 0.201 | 0.215 | 0.636 |
| PCB-105 | 0.109* | 0.142* | 0.087 | 0.015 | 0.021 | 0.189 |
| PCB-138 | 0.061 | 0.075 | 0.041 | 0.181 | 0.222 | 0.539 |
| PCB-156 | 0.039 | 0.061 | 0.014 | 0.390 | 0.323 | 0.827 |
| PCB 180 | 0.068 | 0.088 | 0.034 | 0.131 | 0.150 | 0.611 |
| ΣPCB | 0.061 | 0.079 | 0.036 | 0.172 | 0.189 | 0.590 |
| Sum of three mono-ortho PCB (105+118+156) | 0.089* | 0.113 | 0.066 | 0.048 | 0.066 | 0.320 |
| 4,4'-DDT | 0.070 | 0.077 | 0.058 | 0.121 | 0.211 | 0.379 |
| 4,4'-DDE | 0.046 | 0.081 | 0.000 | 0.311 | 0.119 | 0.995 |
| Trans-nonachlor | 0.063 | 0.095 | 0.026 | 0.162 | 0.124 | 0.689 |

* : Significant correlation (2-tailed significance)

TABLE 6.2.28 BIVARIATE CORRELATION BETWEEN PERCENTILE OF HEAD CIRCUMFERENCE AND EXPOSURE

| Percentile of head circumference at NOS | Spearman's rho | | | P-value | | |
|---|---|---|---|---|---|---|
| | All infants (N=499) | Male (N=267) | Female (N=232) | All infants (N=499) | Male (N=267) | Female (N=232) |
| Mercury | 0.059 | 0.043 | 0.073 | 0.189 | 0.482 | 0.266 |
| HCB | 0.094* | 0.144* | 0.036 | 0.036 | 0.019 | 0.589 |
| β-HCH | -0.007 | 0.044 | -0.055 | 0.883 | 0.477 | 0.401 |
| PCB-118 | 0.125** | 0.148* | 0.099 | 0.005 | 0.015 | 0.131 |
| PCB-153 | 0.081 | 0.107 | 0.055 | 0.072 | 0.082 | 0.405 |
| PCB-105 | 0.162** | 0.201** | 0.115 | <0.001 | 0.001 | 0.081 |
| PCB-138 | 0.088* | 0.110 | 0.065 | 0.050 | 0.072 | 0.323 |
| PCB-156 | 0.072 | 0.106 | 0.037 | 0.108 | 0.085 | 0.578 |
| PCB- 180 | 0.084 | 0.113 | 0.052 | 0.062 | 0.065 | 0.429 |
| ΣPCB | 0.084 | 0.110 | 0.059 | 0.060 | 0.073 | 0.370 |
| Sum of three mono-ortho PCB (105+118+156) | 0.122** | 0.152* | 0.089 | 0.006 | 0.013 | 0.176 |
| 4,4'-DDT | 0.113* | 0.140* | 0.088 | 0.011 | 0.022 | 0.183 |
| 4,4'-DDE | 0.079 | 0.105 | 0.054 | 0.079 | 0.088 | 0.417 |
| Trans-nonachlor | 0.103* | 0.127* | 0.077 | 0.021 | 0.038 | 0.245 |

* : Significant correlation (2-tailed significance)
** : Highly significant correlation (2-tailed significance)

TABLE 6.2.29 BIVARIATE CORRELATION BETWEEN BODY LENGTH AND EXPOSURE DATA, ALL CHILDREN

| Body length at NOS | Spearman´s rho | | | P-value | | |
|---|---|---|---|---|---|---|
| | All infants (N=498) | Male (N=267) | Female (N=231) | All infants (N=498) | Male (N=267) | Female (N=231) |
| Mercury | 0.052 | 0.009 | 0.064 | 0.426 | 0.885 | 0.332 |
| HCB | 0.003 | -0.009 | 0.006 | 0.945 | 0.882 | 0.928 |
| β-HCH | -0.035 | -0.046 | -0.003 | 0.431 | 0.458 | 0.969 |
| PCB-118 | 0.054 | 0.032 | 0.089 | 0.226 | 0.604 | 0.178 |
| PCB-153 | 0.011 | -0.018 | 0.052 | 0.813 | 0.765 | 0.436 |
| PCB-105 | 0.062 | 0.043 | 0.093 | 0.170 | 0.486 | 0.160 |
| PCB-138 | 0.032 | -0.004 | 0.078 | 0.476 | 0.950 | 0.236 |
| PCB-156 | 0.002 | -0.041 | 0.053 | 0.970 | 0.504 | 0.421 |
| PCB-180 | 0.015 | -0.013 | 0.049 | 0.736 | 0.832 | 0.461 |
| ΣPCB | 0.017 | -0.014 | 0.059 | 0.698 | 0.816 | 0.371 |
| Sum of three mono-ortho PCB (105+118+156) | 0.045 | -0.017 | 0.085 | 0.316 | 0.779 | 0.199 |
| 4,4'-DDT | 0.020 | 0.021 | 0.023 | 0.659 | 0.727 | 0.724 |
| 4,4'-DDE | 0.001 | -0.017 | 0.027 | 0.981 | 0.782 | 0.682 |
| Trans-nonachlor | 0.039 | 0.021 | 0.057 | 0.379 | 0.738 | 0.387 |

TABLE 6.2.30 BODY LENGTH AND EXPOSURE DATA: PARTIAL CORRELATION, CONTROLLED FOR AGE AT NOS, FOR MATERNAL WEIGHT AND HEIGHT, FOR PARITY, LOG10 OF PCB 105 - ALL CHILDREN)

| Body length at NOS | Partial correlation coefficients | | | P-value | | |
|---|---|---|---|---|---|---|
| | All infants (N=498) | Male (N=267) | Female (N=231) | All infants (N=498) | Male (N=267) | Female (N=231) |
| Mercury | -0.017 | -0.061 | 0.008 | 0.708 | 0.323 | 0.901 |
| HCB | -0.128** | -0.165** | -0.100 | 0.004 | 0.008 | 0.133 |
| β-HCH | -0.096* | -0.133* | -0.014 | 0.032 | 0.031 | 0.840 |
| PCB-118 | 0.025 | -0.021 | 0.060 | 0.574 | 0.735 | 0.372 |
| PCB-153 | -0.072 | -0.127* | -0.009 | 0.108 | 0.039 | 0.890 |
| PCB-138 | -0.049 | -0.109 | 0.023 | 0.274 | 0.079 | 0.729 |
| PCB-156 | -0.073 | -0.150* | 0.018 | 0.104 | 0.015 | 0.784 |
| PCB-180 | -0.038 | -0.100 | 0.024 | 0.397 | 0.106 | 0.719 |
| 2 x sum of PCB (138+153+180) | -0.058 | -0.117 | 0.009 | 0.189 | 0.059 | 0.894 |
| Sum of PCB (138+153+156) | -0.064 | -0.122* | 0.005 | 0.158 | 0.049 | 0.936 |
| Sum of three mono-ortho PCB (105+118+156) | -0.017 | -0.063 | 0.029 | 0.705 | 0.109 | 0.660 |
| 4,4'-DDT | -0.097* | -0.089 | -0.130* | 0.032 | 0.153 | 0.050 |
| 4,4'-DDE | -0.115* | -0.140* | -0.107 | 0.011 | 0.024 | 0.107 |
| Trans-nonachlor | -0.050 | -0.046 | -0.046 | 0.264 | 0.454 | 0.496 |

* : Significant correlation (2-tailed significance)
** : Highly significant correlation (2-tailed significance)

TABLE 6.2.31 PARTIAL CORRELATION BETWEEN NOS AND EXPOSURE DATA, COHORT DIVIDED AFTER SEX (CORRECTED FOR CORRECTED AGE AT NOS, ENVIRONMENTAL TEMPERATURE, INTERVAL TO LAST MEAL, AND WEIGHT GAIN OF MOTHER DURING PREGNANCY)

| | NOS (all infants) (N=500) | | NOS (all boys) (N=267) | | NOS (all girls) (N=233) | |
|---|---|---|---|---|---|---|
| | Partial Correlation Coefficient | P-value | Partial Correlation Coefficient | P-value | Partial Correlation Coefficient | Pp-value |
| Log10 MeHg | -0.031 | 0.518 | 0.056 | 0.392 | -0.130 | 0.061 |
| Log10 HCB | -0.098 | **0.037** | -0.174 | **0.007** | -0.005 | 0.940 |
| Log10 β-HCH | -0.025 | 0.591 | -0.161 | **0.013** | 0.161 | **0.020** |
| Log10 musk xylene | -0.054 | 0.255 | -0.037 | 0.568 | -0.062 | 0.372 |
| Log10 PCB 118 | -0.078 | 0.097 | -0.128 | **0.049** | -0.024 | 0.725 |
| Log10 PCB 153 | -0.078 | 0.099 | -0.119 | 0.068 | -0.030 | 0.665 |
| Log10 PCB 105 | -0.101 | **0.032** | -0.152 | **0.019** | -0.044 | 0.525 |
| Log10 PCB 138 | -0.071 | 0.132 | -0.116 | 0.075 | -0.018 | 0.791 |
| Log10 PCB 156 | -0.042 | 0.372 | -0.081 | 0.215 | -0.001 | 0.985 |
| Log10 PCB 180 | -0.069 | 0.143 | -0.112 | 0.086 | -0.024 | 0.732 |
| Log10 DDE | -0.084 | 0.075 | -0.129 | **0.047** | -0.032 | 0.649 |
| Log10 DDT | -0.093 | **0.049** | -0.140 | **0.031** | -0.041 | 0.554 |
| Log10 trans-nonachlor | -0.056 | 0.239 | -0.093 | 0.155 | -0.010 | 0.891 |

TABLE 6.2.32 LINEAR REGRESSION MODEL FOR NOS (EXAMINER B ONLY)

MODEL SUMMARY

| | R | $R^2$ | Adjusted $R^2$ | Standardized error of the estimate |
|---|---|---|---|---|
| For all children seen by ST | 0.522 | 0.273 | 0.228 | 3.00 |
| For all boys seen by ST* | 0.752 | 0.566 | 0.514 | 2.39 |

| | Unstandardized coefficients | | Standardized coefficients | Significance | | Collinearity statistic (tolerance) |
|---|---|---|---|---|---|---|
| | B | Standard error | Beta | ♀+♂ (N=233) | ♂ (N=131) | |
| Constant | 56.84 | 7.444 | | **<0.001** | **<0.001** | |
| Corrected age at NOS (days) | -0.102 | 0.037 | -0.172 | **0.007** | **0.002** | 0.949 |
| Interval to last meal (min) | 0.012 | 0.005 | 0.163 | **0.009** | **0.042** | 0.977 |
| Environmental temperature (°C) | -0.391 | 0.276 | -0.088 | 0.159 | **0.001** | 0.970 |
| Stability of states (no / yes) | 5.082 | 1.404 | 0.230 | **<0.001** | **<0.001** | 0.935 |
| Level of higher one of parents´ profession/ occupation (low/ high) | -0.877 | 0.447 | -0.128 | 0.051 | 0.138 | 0.879 |
| Weight gain during pregnancy (kg)* | -0.038 | 0.040 | -0.059 | 0.351 | Not in model | 0.944 |
| Early abortions (no / yes) | -0.797 | 0.501 | -0.102 | 0.114 | 0.051 | 0.909 |
| Log10 of MeHg | 1.125 | 0.595 | 0.140 | 0.060 | **0.002** | 0.688 |
| Log10 of HCB | -3.155 | 2.179 | -0.206 | 0.149 | 0.117 | 0.186 |
| Log10 of PCB 105 | -2.356 | 0.973 | -0.286 | **0.016** | **0.001** | 0.269 |
| Log10 of PCB 156 | 10.72 | 2.804 | 0.984 | **<0.001** | **<0.001** | 0.057 |
| Log10 of PCB 180 | -8.207 | 2.603 | -0.787 | **0.002** | **0.007** | 0.059 |
| Log10 of t-nonachlor* | --- | --- | --- | --- | 0.312 | --- |

* : Same model as for all children seen by B with trans-nonachlor instead of weight gain

TABLE 6.2.33 CORRELATION BETWEEN HYPOKINESIA AND EXPOSURE DATA* (T-TEST)

| Hypokinesia (no / yes) | All children (N=500) | | All boys (N=267) | | All girls (N=233) | |
|---|---|---|---|---|---|---|
| | T-value | Sig. (2-tailed) of t-value | T-value | Sig. (2-tailed) of t-value | T-value | Sig. (2-tailed) of t-value |
| Mercury | 1.562 | 0.119 | 2.089 | **0.038** | 0.171 | 0.867 |
| HCB | -0.648 | 0.517 | -0.403 | 0.687 | -0.518 | 0.605 |
| β-HCH | 0.014 | 0.989 | -1.037 | 0.301 | 1.229 | 0.220 |
| Musk xylene | -0.441 | 0.659 | -0.683 | 0.524 | 0.022 | 0.983 |
| PCB-118 | -2.562 | **0.017** | -0.975 | 0.330 | -2.886 | **0.012** |
| PCB-153 | -2.436 | **0.022** | -0.875 | 0.382 | -2.430 | **0.031** |
| PCB-105 | -2.422 | **0.023** | -1.024 | 0.307 | -2.133 | 0.055 |
| PCB-138 | -2.389 | **0.025** | -0.879 | 0.380 | -2.484 | **0.029** |
| PCB-156 | -2.088 | **0.047** | -0.756 | 0.450 | -1.975 | 0.069 |
| PCB-180 | -2.422 | **0.023** | -0.806 | 0.421 | -2.615 | **0.021** |
| ΣPCB | -2.461 | **0.021** | -0.868 | 0.386 | -2.562 | **0.024** |
| Sum of three mono-ortho PCBs (105+118+156) | -2.472 | **0.021** | -0.946 | 0.345 | -2.659 | **0.019** |
| 4,4'-DDE | -1.726 | 0.085 | -0.620 | 0.536 | -1.840 | 0.067 |
| 4,4'-DDT | -2.754 | **0.011** | -1.084 | 0.279 | -2.450 | **0.031** |
| Trans-nonachlor | -3.171 | **0.004** | -1.669 | 0.120 | -2.956 | **0.011** |

* : All exposure variable were tested as log10-transformed values

TABLE 6.2.34 BIVARIATE CORRELATION BETWEEN REFLEX CLUSTER SCORE AND EXPOSURE DATA

| Exposure variable | Complete cohort (N=500) | | Subcohort B (N=233) | |
|---|---|---|---|---|
| | Spearman´s rho | p-value | Spearman´s rho | P-value |
| Mercury | 0.034 | 0.447 | -0.016 | 0.807 |
| HCB | -0.045 | 0.315 | -0.158 | **0.016** |
| β-HCH | -0.087 | 0.053 | -0.177 | **0.007** |
| PCB-118 | -0.044 | 0.325 | -0.194 | **0.003** |
| PCB-153 | -0.038 | 0.402 | -0.185 | **0.005** |
| PCB-105 | -0.024 | 0.593 | -0.158 | **0.016** |
| PCB-138 | -0.038 | 0.396 | -0.188 | **0.004** |
| PCB-156 | -0.036 | 0.422 | -0.150 | **0.022** |
| PCB-180 | -0.042 | 0.351 | -0.177 | **0.007** |
| 2 x sum of PCB (138+153+180) | -0.039 | 0.390 | -0.187 | **0.004** |
| 4,4'-DDT | -0.015 | 0.745 | -0.139 | **0.033** |
| 4,4'-DDE | -0.019 | 0.673 | -0.167 | **0.010** |
| T-nonachlor | -0.035 | 0.430 | -0.180 | **0.006** |
| Musk xylene | 0.027 | 0.552 | -0.042 | 0.523 |

Table 6.2.35 Summary of neurological effects, differentiated after sex

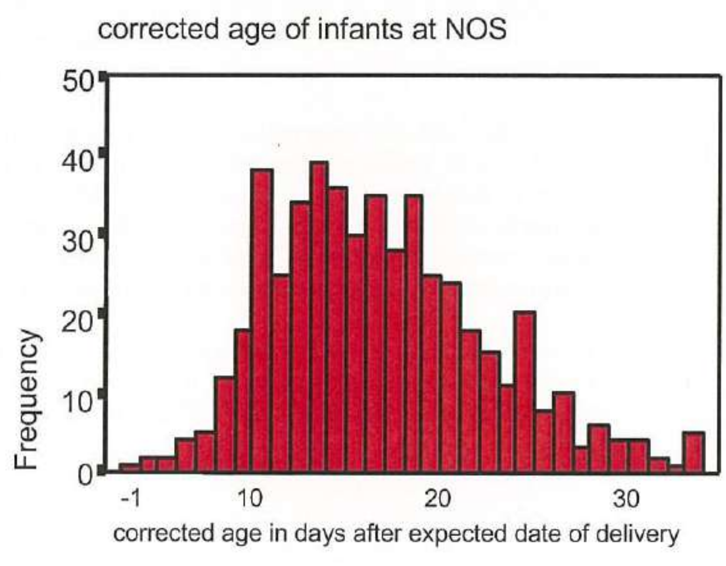
| Contaminant | Effects in male | Effects in female |
|---|---|---|
| Mercury | NOS (↑)<br>Reflex cluster score (↑)<br>Tonus cluster score : 0<br>Much less hypokinesia ↓↓<br>More hyperkinesia (↑)<br>Less opisthotonus (↓) | NOS ↓<br>Relex cluster score (↓)<br>Postural tone cluster score ↓↓<br>No effect on hypokinesia<br>Less hyperkinesia ↓<br>Much less opisthotonus ↓ |
| HCB | NOS ↓↓<br>Reflex cluster score ↓<br>Postural tone cluster score (↓)<br>More hypokinesia (↑)<br>No effect on hyperkinesia<br>Less opisthotonus (↓) | No effect on NOS<br>Reflex cluster score: 0<br>Tonus cluster score: 0<br>More hypokinesia (↑)<br>Hyperkinesia (↑)<br>Less opisthotonus ↓ |
| β-HCH | NOS ↓↓<br>Reflex cluster score ↓↓<br>Postural tone cluster score (↓)<br>More hypokinesia (↑)<br>More hyperkinesia (↑)<br>Less opisthotonus (↓) | NOS ↑↑<br>Reflex cluster score (↓)<br>Postural tone cluster score ↑↑<br>Less hypokinesia ↓<br>Less hyperkinesia (↓)<br>Less opisthotonus (↓) |
| Musk xylene | NOS (↓)<br>Reflex cluster score: no effect<br>Postural tone cluster score (↓)<br>More hypokinesia (↑)<br>Less hyperkinesia (↓)<br>Less opisthotonus (↓) | NOS (↓)<br>Reflex cluster score (↓)<br>No effect on tone score<br>No effect on hypokinesia<br>More hyperkinesia (↑)<br>More opisthotonus (↑) |
| PCB-118 | NOS ↓↓<br>Reflex cluster score ↓<br>Postural tone cluster score ↓<br>More hypokinesia (↑)<br>No effect on hyperkinesia<br>Less opisthotonus (↓) | NOS (↓)<br>Reflex cluster score (↓)<br>Postural tone cluster score (↑)<br>Much more hypokinesia (↑↑)<br>No effect on hyperkinesia<br>Much less opisthotonus ↓↓ |
| PCB-153 | NOS ↓<br>Reflex cluster score ↓<br>Postural tone cluster score (↓)<br>More hypokinesia (↑)<br>No effect on hyperkinesia<br>Less opisthotonus (↓) | NOS (↓)<br>Reflex cluster score (↓)<br>Postural tone cluster score (↑)<br>Much more hypokinesia ↑↑<br>No effect on hyperkinesia<br>Much less opisthotonus ↓↓ |
| PCB-105 | NOS ↓↓<br>Reflex cluster score (↓)<br>Postural tone cluster score (↓)<br>More hypokinesia (↑)<br>Less hyperkinesia (↓)<br>Less opisthotonus (↓) | NOS (↓)<br>Reflex cluster score (↓)<br>Postural tone cluster score (↑)<br>Much more hypokinesia ↑<br>No effect on hyperkinesia<br>Less opisthotonus (↓) |
| PCB-138 | NOS ↓<br>Reflex cluster score ↓<br>Postural tone cluster score (↓)<br>More hypokinesia (↑)<br>More hyperkinesia (↑)<br>Less opisthotonus (↓) | No effect on NOS<br>Reflex cluster score (↓)<br>Postural tone cluster score (↑)<br>Much more hypokinesia ↑↑<br>No effect on hyperkinesia<br>Much less opisthotonus ↓↓ |

| | | |
|---|---|---|
| PCB-156 | NOS ↓<br>Reflex cluster score (↓)<br>Postural tone cluster score (↓)<br>More hypokinesia (↑)<br>No effect on hyperkinesia<br>Less opisthotonus (↓) | No effect on NOS<br>Reflex cluster score (↓)<br>Postural tone cluster score (↑)<br>Much more hypokinesia ↑<br>No effect on hyperkinesia<br>Much less opisthotonus ↓↓ |
| PCB-180 | NOS ↓<br>Reflex cluster score ↓<br>Postural tone cluster score ↓<br>More hypokinesia (↑)<br>No effect on hyperkinesia<br>Less opisthotonus ↓ | NOS (↓)<br>Reflex cluster score (↑)<br>Postural tone cluster score (↑)<br>Much more hypokinesia ↑↑<br>No effect on hyperkinesia<br>Much less opisthotonus ↓↓ |
| DDE | NOS ↓↓<br>Reflex cluster score (↓)<br>Postural tone cluster score (↓)<br>More hypokinesia (↑)<br>No effect on hyperkinesia<br>Less opisthotonus (↓) | NOS (↓)<br>Reflex cluster score (↓)<br>Postural tone cluster score (↑)<br>Much more hypokinesia ↑<br>No effect on hyperkinesia<br>Much less opisthotonus ↓↓ |
| DDT | NOS ↓↓<br>Reflex cluster score (↓)<br>Postural tone cluster score (↓)<br>More hypokinesia (↑)<br>More hyperkinesia (↑)<br>No effect on opisthotonus | NOS (↓)<br>Reflex cluster score: no effect<br>Postural tone cluster score (↑)<br>Much more hypokinesia ↑<br>No effect on hyperkinesia<br>Much less opisthotonus ↓↓ |
| Tans-nonachlor | NOS ↓<br>Reflex cluster score (↓)<br>Postural tone cluster score (↓)<br>More hypokinesia ↑<br>More hyperkinesia (↑)<br>Less opisthotonus (↓) | No effect on NOS<br>Reflex cluster score (↓)<br>Postural tone cluster score (↑)<br>Much more hypokinesia ↑↑<br>More hyperkinesia (↑)<br>Much less opisthotonus ↓↓ |

↑↑/•• : Significance of t- resp. p-value <0.050
↑/• : Significance of t- resp. p-value 0.050 – 0.250
(↑)/(•) : Significance of t- resp. p-value 0.251 – 0.750
— : Significance of t- resp. p-value > 0.750
o : No effect

### 6.2.7.3 *Figures*

FIGURE 6.2.4 DISTRIBUTION OF CORRECTED AGE OF INFANTS IN DAYS (AGE AFTER EXPECTED DATE OF DELIVERY, WHICH WAS CALCULATED AFTER LAST MENSTRUAL PERIOD) AT NEUROLOGICAL EXAMINATION.



### 6.3.1 Material and Methods:

In August 1998 Faroese health authorities recommended women to reduce their intake of pilot whale meat and blubber in order to protect the foetus against adverse effects from food contaminants. This study describes the effects of this recommendation. To cover the daily variations we used 24 hour recall (24 h recall), as well as a food diary (FD), where all food consumed during one day at a time was reported. To adjust for seasonal variations the women answered a food frequency questionnaire (FFQ) where what is considered Faroese food was listed and we asked about consumption during the past 12 months. General information about height, weigh and smoking and drinking habits, previous deliveries and educational level were recorded. Blood samples were taken in the $37^{th}$ week of pregnancy and analysed for heavy metals and organochlorines. The registration sheets were in accordance with a previously performed dietary survey in the Faroes and in accordance with datasheets approved upon in the human health group of AMAP.

In the Faroe Islands there are three delivering units, one main unit at the main hospital in Tórshavn and the other two at hospitals in Tvøroyri and Klaksvík. When a woman becomes pregnant, the GP reports this to the delivering unit where she is expected to give birth. We used these lists with names, ID numbers, addresses and term dates to enter the participants in a data base designed for this purpose, and each subject was assigned her own file number. A standard letter, where the purpose of this study was explained and how we were obtaining the information, was sent to the women when they were 24-26 weeks pregnant. They could respond themselves by returning the signed form but often we contacted them by telephone approximately one week after the letters were sent, to provide further information and ask if they wanted to participate. We sent letters for one month at a time.

The data collection was done for 51 weeks, from Oct. 2000 until Sep. 2001. Two individuals served as interviewers, one clinical dietician and one trained midwife. During this period there were a total of 486 pregnant women and 298 = 65,6% were invited to participate. 100 women did not want to participate, but did not give any specific reason, 3 women had had a miscarriage, in 2 women the term date did not equal the list we had and they were too close to term date and 4 women were abroad. A total of 189 (66,4%) agread to participate. During the investigation period 8 subjects (2,7%) did not want to continue, 14 subjects (4,7%) did not take the blood sample and dropped out, 10 subjects (3,4%) did accept to participate but an appointments was not made and 9 subjects (3%) did accept to participate but we could not accommodate the interviews because of lack of time. We ended up with 148 (49.7%), who participated in the entire project.

Data Collection: We interviewed the women at home when they were about 28, 33 and 38 weeks pregnant. They received a telephone call the evening before to make an appointment, at 8:30–10:00 p.m. The usual time for supper in the Faroe Islands is around 6:30 p.m. and by calling them at this time we assumed that most of the meals that day already had been consumed. In some cases we called the morning of the interview.

To estimate the amount consumed we used (food) models and pictures completed with instructions where the weight of the food was defined in proportion to the models/pictures. These models and matching instructions

were borrowed from The National Food Agency in Denmark. We made models for Faroese food items as needed.

First visit: 24 h recall, starting with first item consumed the previous day and during the next 24 hours in the order of time of consumption, what was consumed and how much according to the food models. Then the Food Frequency Questionaire (FFQ) was answered and the questionnaire on general questions. Sheets for Food Diary (FD) for 3 days were handed out with a detailed explanation about recording everything consumed during the days agreed upon. We included always one weekend in the FD.

Second visit: 24 h recall questionnaire performed as at the first visit. The FD recording was checked with the subjects using the models to quantify the consumption. FD-recording sheets for three more days were handed out.

Third visit: 24 h recall questionaire performed and the Food Diary checked with the subjects.

All together there were obtained 409 24h recall interviews from the 148 women (116 did all three interviews, 29 two interviews and 3 women only one interview). The main reason for not doing all three interviews was delivery and scheduling difficulties.

In total 732 FD recordings were collected (in average five FD´s per woman. The reasons for not doing all six were mainly delivery and lack of motivation. Altogether this totals 1,141 recordings.

Before the data collection started we completed 17 interviews as pilot tests covering all parts of our concept, equally divided between the interviewers and mutually observed. During the collection period we tried to keep the participants separate so that the interviewer who started also finished each participant, but for different reasons this was not possible for all women. A total of 97 women only had one interwiever as intended and 51 saw both interviewers during the data collection phase. 26 times the interviewers supervised each other, and weekly meetings ensured continuity of data quality.

After each home visit all food items were estimated according to the models and recorded with name of item and matching weight on a sheet designed for this purpose. When all data collection was done the clinical dietician reviewed all 1,141 recordings to confirm all data and ensured consistency.

Data entering: After confirming of all the data two assistants were reading while the interviewers keyed in all the data. For data entering we used the dietary evaluation soft-ware Dankost 3000. The calculation is based on Atwater. This program calculates the macro- and micronutrients. Food items, which did not exist in Dankost 3000 beforehand, were entered form Faroese- and Icelandic food records. For some food items we used the declaration on the package. For many of the items entered the only available information was the macronutrients and a few micronutrients. In some cases, mostly sweets with no declaration on the package, the clinical dietician decided which food item with known values came the closest. For statistical purposes data were exported to ACCESS and SPSS.

### 6.3.2 Results

*6.3.2.1 Lifestyle factors among 165 pregnant women according to the food frequency questionnaire (AMAP questionnaire), administered by the interviewers:*

SAMPLE CARACTERISTICS:

| Number | Age median (min-max) | Height in cm mean (min-max) | Weight in kg median (min-max) |
|---|---|---|---|
| | 29 (17-40) | 165.8 (150-183) | 65.2 (47-115) |

SMOKING:

| Number of valid questionnaires: 165 | Never smoked | Former smoker | Present smoker | Occasional smoking |
|---|---|---|---|---|
| Number (%) | 84 (51%) | 38 (23%) | 30 (18%) | 13 (8%) |
| Cigarettes per day, mean (min-max) | - | 6.6 (1-20) | 7.7 (2-15) | 2 (1-3) |
| Years smoking, mean (min-max) | - | 3.6 (1-5) | 4.2 (2-6) | 3.9 (2-5) |

ALCOHOL CONSUMPTION IN PREGNANCY:

| Trimester of Pregnancy | Bottles of beer per month mean (max); Std. Dev. | Glasses of wine per month mean (max); Std. Dev. | Shots of liquor per month mean (max); Std. Dev. |
|---|---|---|---|
| First | 1.05 (24); 2.7 | 0.98 (18); 2.10 | 0.75 (19) ; 2.47 |
| Second | 0.30 (6); 0.83 | 0.72 (8); 1.23 | 0.25 (20); 1.66 |

38,3 % Reported to be total abstainers in first trimester of pregnancy
49,7 % Reported to be total abstainers in second trimester of pregnancy

PILOT WHALE FOR DINNER IN AVERAGE DURING THE LAST 12 MONTHS:

| N= 157 | |
|---|---|
| Once a month or less | 2-3 times per month |
| 154 (92.2%) | 3 (1.8%) |

OCEAN FISH FOR DINNER IN AVERAGE DURING THE LAST 12 MONTHS:

| N=155 | | | |
|---|---|---|---|
| Once per month or less | 2-3 times per month | 1-3 times per week | 4 times or more per week |
| 5 (3.0 %) | 26 (15.6%) | 93 (55.7%) | 31 (18.6%) |

BIRDS FOR DINNER IN AVERAGE DURING THE LAST 12 MONTHS:

| N=154 | | | |
|---|---|---|---|
| Once per month or less | 2-3 times per month | 1-3 times per week | 4 times or more per week |
| 39 (23.4 %) | 80 (47.9 %) | 34 (20.4 %) | 1 (0.6 %) |

*6.3.2.2 Characteristics of the diet based on calculations of the 409 24-h recall interviews and the 732 food diary recordings:*

| | Mean | Minimum | Maximum |
|---|---|---|---|
| Energy per day | 10,231 kJ | 2,878 kJ | 37,766 kJ |
| Protein, % of total energy | 14.7% | 5.7% | 47.3% |
| Lipid, % of total energy | 33.3% | 9.6% | 67.5% |
| Carbohydrates, % of total energy | 51.9% | 23.4% | 75.0% |
| Dietary fibres in grams pr. 1000 kJ | 1.7 g | | |
| Saturated fatty acids per day | 28.8g | 0.78g | 122.5g |
| Monounsaturated fatty acids per day | 21.26g | 0.32g | 139.8g |
| Polyunsaturated fatty acids per day | 9.97g | 0.036g | 73.5g |
| Oceanic fish in average per day | 40.2g | | |
| Pilot whale meat in average pr. day | 1.45g | | |
| Pilot whale blubber in average pr. day | 0.60g | | |
| Sea birds in average pr. day | 3.00g | | |

The dietary intake of pilot whale meat and blubber is remarkably low compared with the last dietary survey in 1981-82, where the average consumption of pilot whale meat among adult men and women was 12 grams per day and of blubber 7 grams. This reduction is most likely to be a result of the recommendations to pregnant women to avoid contaminated seafood, such as pilot whale meat and blubber.

### *6.3.2.3 Contaminants in the blood of the mothers in 38th week.*

MEAN CONCENTRATIONS OF ORGANOCHLORINES IN MATERNAL BLOOD SERUM - WET WEIGHT BASIS (MEANS, UG/L)

| | N | Minimum | Maximum | Mean | Std. Deviation |
|---|---|---|---|---|---|
| A-HCH | 148 | N.d. | N.d. | - | - |
| B-HCH | 148 | N.d. | 0.597 | 0.114 | 0.099 |
| G-HCH | 148 | N.d. | N.d. | - | - |
| Hexachlorbenzol | 148 | .050 | 1.934 | 0.36363 | 0.319 |
| Oxychlordan | 148 | N.d. | 1.427 | 0.159 | 0.196 |
| Cis Chlordan | 148 | N.d. | N.d. | 0.001 | 0.000 |
| Trans-Chlordan | 148 | N.d. | N.d. | 0.001 | 0.000 |
| Nonachlor | 148 | N.d. | 4.221 | 0.671 | 0.826 |
| Toxaphene Parlar 26 | 148 | N.d. | 1.496 | 0.152 | 0.212 |
| Toxaphene Parlar 32 | 148 | N.d. | 0.059 | 0.002 | 0.008 |
| Toxaphene Parlar 44 | 148 | N.d. | 0.326 | 0.030 | 0.052 |
| Toxaphene Parlar 50 | 148 | N.d. | 1.609 | 0.194 | 0.251 |
| P,p-DDE | 148 | 0.351 | 39.438 | 5.534 | 6.051 |
| P,p-DDT | 148 | N.d. | 1.461 | 0.175 | 0.251 |
| PCB-28 | 148 | N.d. | 0.151 | 0.004 | 0.017 |
| PCB-52 | 148 | N.d. | N.d. | - | - |
| PCB-101 | 148 | N.d. | 0.225 | 0.012 | 0.032 |
| PCB-99 | 148 | N.d. | 1.275 | 0.292 | 0.268 |
| PCB-138 | 148 | ,110 | 10.341 | 1.834 | 1.690 |
| PCB-187 | 148 | ,030 | 3.500 | 0.682 | 0.664 |
| PCB-183 | 148 | N.d. | 0.811 | 0.166 | 0.148 |
| PCB-128 | 148 | ,052 | 4.031 | 0.756 | 0.686 |
| PCB-118 | 148 | ,031 | 2.852 | 0.470 | 0.481 |
| PCB-153 | 148 | N.d. | 14.529 | 2.189 | 2.051 |
| PCB-105 | 148 | N.d. | 0.583 | 0.091 | 0.105 |
| PCB-156 | 148 | N.d. | 1.486 | 0.167 | 0.180 |
| PCB-180 | 148 | 0.057 | 7.355 | 1.432 | 1.272 |
| PCB-170 | 148 | N.d. | 4.304 | 0.666 | 0.660 |
| Lipid (mg/dl) | 148 | 394.12 | 1438.43 | 827.01 | 166.97 |

Non-detecable (n.d.) concentrations were assumed to be 0.001 ug/l

MEAN CONCENTRATIONS OF METALS IN MATERNAL BLOOD, WHOLE WEIGHT BASIS (MEANS UG/L)

| Metal | N | Minimum | Maximum | Mean | Std. Deviation |
|---|---|---|---|---|---|
| Lead | 124 | 13.3 | 99.8 | 22.46 | 10.0 |
| Cadmium | 124 | 0.020 | 2.90 | 0.42 | 0.46 |
| Mercury (total) | 124 | 0.001 | 7.50 | 1.86 | 1.4 |
| Selenium | 121 | 54 | 169 | 102.1 | 23.9 |

### 6.3.3 Discussion:

The PCB concentrations are elevated, as seen in other studies among pregnant women in the Faroes. In 1994 the sum of PCBs (geometric mean of (PCB 138+153+180) * 2 was 1.12 μg/g lipid. The corresponding value from this study is 0.94 μg/g lipid. The reduction of PCB´s in pregnant women is moderate compared to reduction of mercury, which is dramatic. Cord blood mercury concentrations in 1,023 births in 1986/87 was 24,2 μg/l (median). In this study the median is only 1,4 μg/l.

The results from the dietary survey showed a very significant reduction in whale meat and blubber intake, and blood analysis shows a corresponding reduction in the mercury exposure. However, the PCB levels are still high and must be considered to be a potential health problem in the Faroese community. According to the dietary survey the daily intake of both whale meat and whale blubber has been reduced up to one order of magnitude. However, the concentration of organochlorines has not declined to the same extent as the mercury, indicating that organochlorines can have other significant sources, e.g. seabirds. The longer half-life of most of some organochlorines compared to methylmercury may be too be an explanation of this observation.

## 6.4 Exposure to Seafood Contaminants and Immune Response in Faroese Children

From the fall of 2000 the youngest subset of Cohort 3 (N = 130) was invited for a check-up before and after the scheduled childhood vaccination at age 12 months. All infants had followed the normal vaccination program for Danish and Faroese children and were vaccinated with tetanus toxoid (TT), diphtheria toxoid (DT), pertussis toxin (acellular pertussis antigen), polio (inactivated polio virus I, II and III) mixed in one syringe, and *Haemophilus influenzae* type b polysaccharide (HibCP) conjugated to TT (ActHib®) in another. Vaccinations were given approximately at the ages of 3 months, 5 months and 12 months. Serum antibody concentrations against TT, DT and HibCP were determined at the State Serum Institute in Copenhagen, which also produced the vaccines and delivered ActHib (from Avantis Pasteur). TT and DT are classical protein antigens depending on a T-cell help for both primary and recall antibody responses (T-cell dependent antigens). In contrast, as a polysaccharide antigen coupled to a protein carrier (TT), HibCP relies on T-cell function for the primary activation of naive B-cells in infants, while boosting of the response in connection with subsequent vaccination can be elicited by the capsular polysaccharide alone (T-independent activation). The results of this study will be available in the near future.

## 6.5 Exposure to mercury and organochlorines 1985-2001.

### 6.5.1 Introduction

Several large studies have taken place in the Faroe Islands (table 6.5.1) to examine the effects of contaminated seafood on pregnancy outcome and neurodevelopment. A total of five cohorts with 2,400 persons were generated. Exposure data obtained in these studies are collected in this section in a way to provide the best possible basis for comparison of exposure levels of the

different groups during the 15-year period. A summary of the most important characteristics of the study cohorts can be found in table 19 in this section (Description of study populations). The exposure variables are listed in the following paragraphs.

TABLE 6.5.1 LIST OF STUDIES

| | |
|---|---|
| 1 | Pilot study in 1985 |
| 2 | Study on the effects of antenatal exposure to methylmercury (cohort 1: 1986/1987) |
| 3 | Study on the effects of pre- and postnatal exposure to methylmercury and PCB (cohort 2: 1994/5) |
| 4 | Study about the effects of prenatal exposure to methylmercury and organochlorines (cohort 3: 1998/2000) |
| 5 | Intervention study with questionnaires and hair samples about diet in 1999 and 2000 |
| 6 | Dietary Survey of Faroese Women in 3rd Trimester of Pregnancy, 2000/2001 |

### 6.5.2 Mercury in maternal blood

Analyses of total and inorganic mercury in whole blood and serum in the 53 women living in Leirvík of the pilot study in 1985 resulted in the following values (Grandjean et al., 1992):

TABLE 6.5.2

| | N | Median in nmol/L (μg/L) | Range In nmol/L (μg μ/L) |
|---|---|---|---|
| Whole blood: total mercury | 53 | 60 (12.1) | 13 – 250 (2.6 – 50.1) |
| Whole blood: inorganic mercury | 47 | 10.5 | <0.5 – 25 |
| Serum: total mercury | 50 | 10.5 | <0.5 – 41 |
| Serum: inorganic mercury | 52 | 8.5 | <0.5 – 1.5 |

Inorganic mercury represented an average of 11.0 ± 1.85% of the total mercury concentration (Grandjean et al., 1992).

In the following cohort, mercury in maternal hair and in umbilical cord blood were used as biomarker for the exposure during pregnancy.

### 6.5.3 Mercury in maternal hair samples

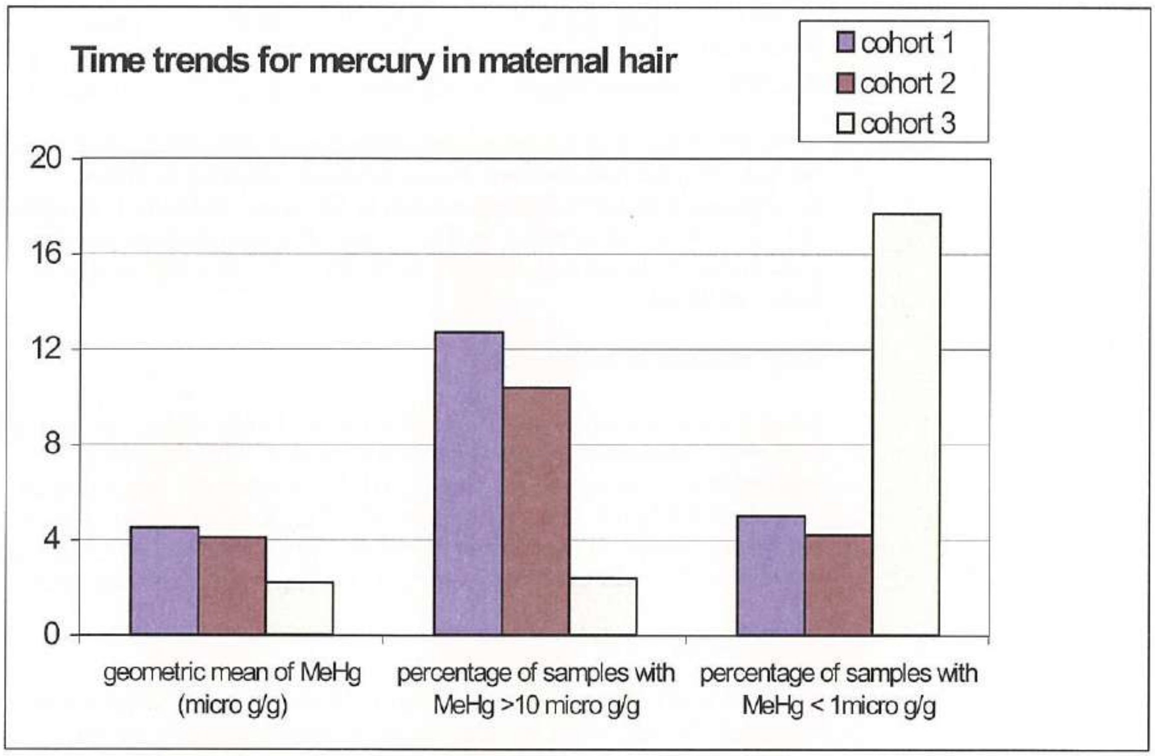
The geometric average hair-mercury concentration in 1,020 Faroese women from Cohort 1 (children born in 1986/1987) was 4.5 μg/g, with 130 samples (12.7%) above 10 μg/g (50 nmol/g). Five samples (0.5%) exceeded 25 μg/g (125 nmol/g). The maximum was 39.1 μg/g (195 nmol/g). Only 5% of the Faroese women from Cohort 1 had hair-mercury concentrations below 1 μg/g. Compared to Cohort I, a slightly lower mercury concentration was found in Cohort 2, with a geometric mean of 4.1 μg/g. Fifteen hair samples (10.4%) exceeded a mercury concentration of 10 μg/g (Steuerwald et al., 2000).

The most recently established cohort (cohort 3) showed a geometric mean for mercury in maternal hair of 2.2 μg/g. In this cohort, which was created in the years 1998 to 2000, only 2.4% (15 of 617) had a mercury concentration above 10 μg/g while in 17.7% (109/617) the concentration was below 1 μg/g (See section 6.2.).

TABLE 6.5.3 MERCURY IN MATERNAL HAIR (μG/G)

| | N | Mean | Median | Geometric mean | P25 | P75 | Mini-mum | Maxi-mum |
|---|---|---|---|---|---|---|---|---|
| Cohort 1 (Grandjean et al., 1992) | 1,020 | 5.6 | 4.6 | 4.5 | 2.5 | 7.7 | 0.17 | 39.1 |
| Cohort 2 (Steuerwald et al., 2000) | 144 | 5.3 | 4.5 | 4.1 | 2.5 | 7.4 | 0.36 | 16.3 |
| Cohort 3 (See section 6.2.) | 617 | 3.1 (SD 3.2) | 2.2 | 2.2 (SD 2.5) | 1.2 | 4.0 | 0.02 | 32.7 |

FIGURE 6.5.1: TIME TRENDS FOR MERCURY IN MATERNAL HAIR



### 6.5.4 Mercury in umbilical cord blood

In cohort 1, the geometric mean for the mercury concentration in umbilical cord blood was 24.2 µg /L. 250 of the 1,023 samples (25.1%) had a blood-mercury concentration that exceeded 40 µg /L (200 nmol/L). Twenty samples (2.0%) exeeded 100 µg /L (500 nmol/L) (Grandjean et al., 1992). The highest level that was measured for this cohort was 351 µg /L (1,755 nmol/L) (Weihe et al., 1996). Again, the concentrations measured in cohort 2, which was established eight years after cohort 1, were slightly lower: the geometric mean for mercury in cord blood reached 20.4 µg /L (Steuerwald et al., 2000).

TABLE 6.5.4 MERCURY IN UMBILICAL CORD BLOOD (µG/L)

| | N | Geometric mean | Median | P25 | P75 |
|---|---|---|---|---|---|
| Cohort 1 (Grandjean et al., 1992) | 894 | 22.9 | 24.2 | 13.0 | 40.2 |
| Cohort 2 (Steuerwald et al., 2000) | 163 | 20.4 | 21.0 | 11.8 | 40.0 |

Cord blood mercury concentrations from cohort 3 are being analyzed and are not yet available for reporting. For comparison the total mercury concentration in 124 pregnant women in $38^{th}$ week was only 1,26 microgram/l in Cohort 4 (see section 6.3. in this report). For comparison, mercury concentrations in cord blood are usually about 25-50% higher than in maternal blood.

### 6.5.5 Mercury in breast milk

During a one-month period (Grandjean et al., 1992) 88 samples of transition milk were collected from mothers from Cohort 1. Total mercury concentration was between 1 and 4 µg /L for most of the samples with a median of 2.45 µg/L and a maximum of 8.7 µg /L (Grandjean et al., 1995). No further results of mercury in breast milk are available, but the results suggest that human milk may contribute an important exposure source.

### 6.5.6 MeHg in hair in children

Of about half of the cohort 1-children (583 children or 57.0%) a hair sample of at least 100 mg could be obtained at the age of about 12 months (Grandjean et al., 1994). A second sample of the children was collected when they were 7 years old. At that age the geometric mean for methylmercury was nearly threefold the concentration found at the age of one year (Grandjean et al., 1999).

TABLE 6.5.5 METHYLMERCURY IN CHILDREN'S HAIR AT DIFFERENT AGES (IN µG/G)

| (MeHg in µg/g) | Cohort 1 at 12 months (Grandjean et al., 1994) | Cohort 1 at 7 years (Grandjean et al., 1999) |
|---|---|---|
| number of samples | 583 | 903 |
| geometric mean | 1.10 | 2.99 |
| P25 | 0.66 | 1.70 |
| P75 | 1.88 | 6.10 |
| Maximum | 8.82 | 37.61 |

### 6.5.7 Mercury in children at age 7 years

In 672 children out of the 1,024 children of cohort 1, a blood sample was analyzed at 7 years. The geometric mean for mercury was 8.82 µg /L with an interquartile range of 4.8 to 18.2 µg /L (Grandjean et al., 1999). Children from cohort 2 have just reached 7 years, and blood samples are being

collected. However, no comparable data for this age group are available at the moment.

### 6.5.8 PCB in maternal serum

Maternal serum was collected at week 32 of pregnancy for cohort 2 and at week 34 – 36 for cohort 3. In cohort 2, the geometric mean of ΣPCB (sum of 28 PCB congeners, namely IUPAC nos. 28, 52, 56, 66, 74, 99, 101, 105, 110, 118, 138, 146, 153, 156, 170, 172, 177, 178, 180, 183, 189, 193, 194, 195, 201, 203, and 206) was 0.86 µg/g lipid (Grandjean et al., 2001). Results of the analysis of the samples collected for cohort 3 are not available yet.

TABLE 6.5.6 SUM OF PCB IN MATERNAL SERUM

| | | ΣPCB (in µg/g lipid) | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | N | Mean | Median | Geometric mean | P25 | P75 | Minimum | Maximum |
| Cohort 2-1994 (Steuerwald et al., 2000) | 173 | 1.58 | 1.15 | 1.12 | 0.62 | 1.87 | 0.04 | 18.4 |
| Cohort 4-2001 (see section 6.3) | 148 | 1.33 | 0.92 | 0.94 | 0.54 | 1.55 | 0.06 | 8.0 |

[1]: Sum of PCB was calculated as 2.0 times the sum of the most prevalent congeners 138, 153, and 180. While analyzing the PCB concentration in transitional milk of cohort 1, it was found that the three congeners (138, 153, and 180) constituted 50% of the total PCB concentration.

### 6.5.9 PCB in cord blood

For cohort 2 cord blood values of ΣPCB are available, but not for the other cohorts. Results are not published. But the relation between lipid-based PCB values in maternal and cord serum samples is about 1:1 (Steuerwald et al., 2000). Thus the magnitude of the values in cord blood can be estimated when using the numbers given in table 5. In Cohort 1, instead of cord blood, 435 umbilical cords were examined for their PCB content. The mean of the measured sum of PCB (calculated as twice the sum of congeners 138, 153, and 180) was 1.12 ng/g wet weight with an interquartile range of 0.57 to 1.55 ng/g. The lipid content of the tissue showed an average of 2.2 mg/g (Grandjean et al., 1997).

### 6.5.10 PCB in breast milk

Four pooled samples collected while establishing cohort 1 in 1987 showed a total PCB concentrations of 1.9 to 3.5 µg/g lipid (Grandjean et al., 1995). PCB in breast milk from day 4-5 in cohort 2 reached a geometric mean of 1.52 µg/g (total range 0.07-18.5 µg/g) (Steuerwald et al., 2000). The lipid-based concentrations of PCB in maternal serum were closely associated with those of the corresponding milk sample (r=0.92). The concentrations in transitional milk were generally higher than in maternal serum with the milk/serum ratio being 1.44 (Winnecke, 1999). However, note must be taken that milk analysis results were recovery-adjusted, but serum results were not (average recovering of PCB confiners was about 65%).

TABLE 6.5.7 PCB IN BREAST MILK

| | | ΣPCB (in µg/g lipid) | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | N | Mean | Median | Geometric mean | P25 | P75 | Minimum | Maximum |
| Cohort 2 (Steuerwald et al., 2000) | 168 | 2.17 | 1.53 | 1.52 | 0.87 | 2.52 | 0.07 | 18.5 |
| Cohort 3 (See section 6.2) | 587 | 1.72 (SD ± 1.54) | 1.31 | 1.32 | 0.82 | 2.11 | 0.08 | 17.59 |

[1]: Sum of PCB was calculated as 2.0 times the sum of the most prevalent congeners 138, 153, and 180 (International Union of Pure and Applied Chemistry numbers)

TABLE 6.5.8 SPECIFIC PCB-CONGENERS IN BREAST MILK OF FAROESE MOTHERS (µG/G LIPID)

| | Cohort 2 (n=144)[1] | | Cohort 3 (n=569)[2] | |
|---|---|---|---|---|
| | Arithmetic mean (SD) | Geometric mean | Arithmetic mean (SD) | Geometric mean |
| PCB-105 | 0.035 (0.043) | 0.022 | 0.018 (0.017) | 0.012 |
| PCB-118 | 0.103 (0.138) | 0.067 | 0.082 (0.075) | 0.058 |
| PCB-138 | 0.398 (0.386) | 0.293 | 0.280 (0.261) | 0.213 |
| PCB-153 | 0.445 (0.447) | 0.319 | 0.372 (0.313) | 0.285 |
| PCB-156 | 0.027 (0.026) | 0.013 | 0.027 (0.021) | 0.021 |
| PCB-180 | 0.237 (0.246) | 0.167 | 0.208 (0.183) | 0.159 |

Source: 1: Winnecke, 1999; 2: See section 6.2. in this report
n.a. : not available

### 6.5.11 Lead in cord blood

Lead in cord blood was measured in cohort 1; the median of 1015 samples was 82 nmol/L with P25 at 58 nmol/L and P75 at 106 nmol/L. In the 52 women of the pilot study, whole blood lead was measured with a median of 96 nmol/L (range 39 – 174 nmol/L (Grandjean et al., 1992).

### 6.5.12 Selenium

Blood selenium was analyzed in 1020 cord blood samples of cohort 1. The median was 1.4 µmol/L (110 µg /L) with P25 of 1.27 µmol/L and P75 of 1.55 µmol/L (Grandjean et al., 1992).

84 transition milk samples were analyzed for their selenium content. The concentrations ranged between 6.7 and 38 µg /L with a mean of 19.1 µg /L (Grandjean et al., 1995).

In cohort 2, the mean of cord blood selenium was 1.31 µmol/L (103.4 µg /L) with a standard deviation of 0.18 µmol/L (14.2 µg /L) (Grandjean et al., 2001).

### 6.5.13 Other contaminants in maternal serum

TABLE 6.5.9 OTHER CONTAMINANTS IN MATERNAL SERUM OF FAROESE MOTHERS (µG/G LIPID)

| | Cohort 2 (Steuerwald et al., 2000) |
|---|---|
| *p,p'*-DDE (µg/g lipid) | (N=173)<br>geometric average 0.72<br>P25: 0.40 P75: 1.21<br>range 0.18 – 8.0 |

### 6.5.14 Other contaminants in breast milk

TABLE 6.5.10 MEAN CONCENTRATIONS OF OTHER ORGANOCHLORINES AND PERSISTENT PESTICIDES IN BREAST MILK OF FAROESE MOTHERS (µG/KG LIPID)

| | Cohort 2 (N=168)[1] | | Cohort 3 (N=587)[2] | |
|---|---|---|---|---|
| | Arithmetic mean (SD) | Geometric mean | Arithmetic mean (SD) | Geometric mean |
| *Trans*-nonachlor | 157.8 (197.0) | 78.1 | 151.4 (176.3) | 96.3 |
| p, p'-DDT | 61.1 (70.4) | 38.3 | 35.3 (42.3) | 22.2 |
| p, p'-DDE | 1,310.1 (1,446.7) | 856.1 | 848.9 (953.6) | 591.9 |
| DDE/ DDT* | | | 31.07 (24.15) | |
| HCB | 70.2 (51.1) | 58.4 | 44.8 (28.4) | 38.6 |
| β-HCH | 38.5 (19.1) | 27.5 | 23.6 (16.8) | 20.7 |
| Musk-xylene | 41.4 (26.2) | 33.3 | 16.7 (22.1) | 12.8 |

Source: 1: Steuerwald et al., 2000; 2:See section 6.2 in this report)
* : normal distribution, therefore geometric mean was not calculated

In cohort 2, the range of p,p'-DDT was 0.05 – 13.7 µg/g lipid, P25 and P75 reached 0.49 respective 1.55 µg/g lipid (Steuerwald et al., 2000).

### 6.5.15 Contamination levels in two consecutive pregnancies

It was possible to compare exposure data in two following pregnancies for few mothers in cohort 2: 10 women provided two children from two different pregnancies to the cohort. Birth weight, length at birth and head circumference, length of gestation and maternal pre-pregnancy BMI and weight gain during pregnancy did not differ significantly between the group of earlier and later born infants. Four boys and six girls resulted from the earlier pregnancy, the distribution of gender for the next parity was converted: six boys and four girls.

For nine of the mothers two samples of hair were collected and analyzed for methylmercury. The interval between the first and the second samples ranged from 13 to 23 months (average of 18.8 months). The mean of mercury concentration in the second samples was lower but the difference was not significant. If the values measured in the individual mothers in connection with the earlier and the later pregnancy were compared, in three of them a slightly higher value was found in the second samples. The differences between the first and the second sample were 27.3%, 9.6%, and 1.7%. The decrease in the remaining six sample pairs were 30.3%, 48,5%, 70.1%, 70.7%, 71.0%, and 73.8%.

For analysis of organochlorines one earlier sample of breast milk was missing, thus giving the possibility to compare two milk samples of 9 mothers. The means for the different organochlorines as well as for all the PCB-congeners

were lower in the following pregnancy. But none of the differences was significant. When looking at the individual mothers, musk xylene increased in four mothers, PCB 138 in three mothers, β-HCH, PCB 180, and trans-nonachlor in two, HCB and ΣPCB in one. All other contaminants were lower or at the same concentration in the following pregnancy. This observation finds to the observations of other authors who reported lower values of contamination in the following pregnancy.

### 6.5.16 Influence of dietary recommendation

After the results of the earlier studies became available, new recommendations for consumption of whale products were published by the health authorities (Heilsufrøðiliða Starvsstovan, 1998). To examine the effects of the new recommendations, a questionnaire was sent out to all women residing in the Faroe Islands, aged 26 to 30 years. They were asked about their dietary habits. Those who wanted to could send a sample of hair to be analyzed for mercury. One year later all women were contacted again with the offer to send a new hair sample for analyses. 45.7% of questionnaires could be used for statistical analyses. 370 single hair samples were available taken either after the first or after the second letter. 146 women provided two hair samples. The geometric mean methylmercury in the first samples was 2.57 μg/g (arithmetical mean 3.54 μg/g with a standard deviation of 2.90 μg/g). In the second sample the results were 1.83 μg/g (2.56 μg/g ± 2.22 μg/g). The difference between the two concentrations is highly significant (Man-Withney U-test: $p<0.001$; $CI_{95}$ 0.52 – 1.44) (see section 6.3 in this report).

### 6.5.17 Diet during pregnancy

Data or dietary habits during pregnancy were obtained from the cohorts (table 6.5.10).

In Cohort 2, about 60% og the women had whale meat for dinner, and slightly more than one-half had whale blubber, for dinner at least once per month; Most women (147 or 82.6%) had not changed their dietary habits in this regard during the pregnancy (Grandjean et al., 2001).

TABLE 6.5.11 DIETARY HABITS DURING PREGNANCY

| | Cohort 1 (Grandjean et al., 1992) | Cohort 2 (Grandjean et al., 2001) | Cohort 3 (See section 6.2) | Intervention study |
|---|---|---|---|---|
| Number of whale meat dinners / month | 0 = 208 (20.5%)<br><br>1 = 285 (28.1%)<br>2 = 251 (24.7%)<br>3 = 88 (8.7%)<br>≥4 = 183 (18.0%) | 0 = 48 (12.9%)<br><1 = 48 (27.0%)<br>1 = 45 (25.3%)<br>2 = 30 (16.9%)<br>3 = 14 (7.9%)<br>≥4 = 18 (10.0%) | 0 = 122 (38.4%)<br><1 = 168 (52.8%)<br>1 = 17 (5.4%)<br>2 = 9 (2.8%)<br>3 = 0 (0.0%)<br>≥4 = 2 (0.6%) | 0 = 126 (24.3%)<br><1 = 214 (41.3%)<br>1 = 94 (18.2%)<br>2 = 59 (11.4%)<br>3 = 9 (1.7%)<br>≥4 = 16 (3.1%) |
| Number of blubber dinners / month | N.a. | 0 = 53 (29.8%)<br><1 = 32 (18.0%)<br>1 = 32 (18.0%)<br>2 = 30 (16.9%)<br>≥3 = 31 (17.3%) | 0 = 198 (63.3%)<br><1 = 97 (31.1%)<br>1 = 15 (4.7%)<br>2 = 2 (0.6%)<br>≥3 = 1 (0.3%) | 0 = 201 (39.7%)<br><1 = 161 (31.8%)<br>1 = 74 (14.6%)<br>2 = 44 (8.7%)<br>≥3 = 26 (5.2%) |
| Number of fish dinners / week | 0 = 27 (2.7%)<br><br>1 = 140 (13.7%)<br>2 = 365 (35.8%)<br>≥3 = 488 (47.8%) | 0 = 2 (1.1%)<br><br>1 = 34 (19.1%)<br>2 = 52 (29.2%)<br>≥3 = 90 (50.6%) | 0 = 0 (0.0%)<br><1 = 22 (7.0%)<br>1 = 65 (20.8%)<br>2 = 112 (35.8%)<br>≥3 = 114 (36.4%) | 0 = 2 (0.4%)<br><1 = 11 (2.1%)<br>1 = 117 (22.3%)<br>2 = 179 (34.2%)<br>≥3 = 215 (41.0%) |

*: Some of these women might have been pregnant, but pregnancy was not an inclusion criterion

Unfortunately the questionnaire about the dietary habits during pregnancy differed slightly. Therefore, it is not clear how far the number really represent the same consumption.

In the second cohort, the majority of the participating women resided outside of the capital Tórshavn and it suburbs. The availability of whale meat and blubber was higher in the small villages. Thus lower percentages of mothers who reported no or only few dinners with whale products might not only be caused by the awareness of the women of the potential endangerment related to food and the new recommendation from the national health authorities. The reduced access to whale products might also be have caused lower numbers.

### 6.5.18 Comparison of contamination in Faroese and non-Faroese mothers

When comparing exposure data of Faroese (N=562) and non-Faroese (N=21) women participating in cohort 3 it was found that the level of all contaminants are higher in Faroese mothers except for β-HCH. The difference is highly significant for all measured PCB-congeners and trans-nonachlor. Arithmetic means in Faroese mothers are 1.3-fold to 4.2-fold the means of non-Faroese mothers. β-HCH was twice the value in non-Faroese mothers than in Faroese mothers, the level of significance for the difference was 0.069 (see section 6.2 in this report).

### 6.5.19 Description of study populations

| | Pilot study | Cohort 1 | Cohort 2 | Intervention study | Cohort 3 | Cohort 4 |
|---|---|---|---|---|---|---|
| Main references | Grandjean et al., 1992 | Grandjean et al., 1992 | Steuerwald et al., 2000; Grandjean et al., 2001 | Weihe 2001 (unpublished data) | See section 6.2 | See section 6.3 |
| Period of establish-ing the cohort | December 1985 | 1.3.1986 – 31.12.1987 | 3/1994 – 4/1995 | 2/1999 (first hair samples and questionnaire) 3/2000 (second hair sample) | 12/1997 - 2/2000 | 10/2000-10/2001 |
| Mode of selection | All women in the fertile age group (20 to 50 years old), residing in the small fishing village of Leirvík in the Faroe Islands | Consecutive births at all three hospitals in the Faroe Islands | Consecutive singleton births of mothers residing outside of the Tórshavn area at the hospital in Tórshavn | Questionnaire about diet and twice a request for a hair samples were sent to all women residing in the Faroe Islands, aged 26 to 30 | Consecutive births at the National Hospital in Tórshavn, all mothers included | Consecutive births at all 3 hospitals |
| Number of participants | 53 | 1,022 | 182 | 370 (one hair sample) 146 (two hair samples) 539 (questionnaire) | 656 | 148 |
| Portion of all eligible children born in the period | (84% out of the 63 women of this age group) | 75% | 64% | 31.4% (one hair sample) 12.0% (two hair samples) 45.7% (questionnaire) | 55.3% | 49.7% |
| Maternal age: mean (SD) | N.a. | 26.9 years (range 15– 45) | 28.0 years (± 5.8) | N.a. | 29.2 years (± 5.2) (range 16– 43) | 29 17-40) |
| BMI (kg/m²) mean (range) | N.a. | 22.3 (16.0 – 42.4) | 23.1 (17.0 – 38.6) | N.a. | 23.9 (16.6 – 44.1) | 23.7 |
| Number of teetotaller mothers | N.a. | 771 (75.4%) | 159 (87.4%) | N.a. | 375 (58.6%) | 49.7% (in 2. trim.) |
| Number of non-smokers | N.a. | 614 (60.0%) | 125 (68.7%) | N.a. | 448 (70.0%) | 122 (74%) |

N.a. = Not available

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